

# First case of *Helicobacter pylori* infection resistant to seven antibiotics in Iran

Amin Talebi Bezmin Abadi<sup>[1],[2]</sup> and Ashraf Mohabbati Mobarez<sup>[2]</sup>

[1]. Department of Medical Microbiology, Utrecht University, Utrecht, Netherlands. [2]. Department of Bacteriology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.

## ABSTRACT

Treatment of *Helicobacter pylori* infection with common antibiotics is typically recommended for several digestive conditions, including peptic ulcers. However, reports of resistant *H. pylori* isolates are increasing, and unfortunately, these do not respond to currently available therapeutic regimens. We report the case of a 31-year-old woman with two peptic ulcers in the duodenal antrum. An *H. pylori* strain was isolated, and tested for antibiotic resistance using agar dilution and disk diffusion. The isolated strain was found to be resistant to all seven antibiotics that were tested. Therefore, constant monitoring for antibiotic resistance should be performed prior to initiating antibiotic therapy.

**Keywords:** *Helicobacter pylori*. Antibiotics. Resistance.

## INTRODUCTION

The recognition of *Helicobacter pylori* (*H. pylori*) infection as the main causative agent for gastro duodenal disorders had a drastic effect on related fields of research. As with most bacterial infections, successful treatment of *H. pylori* infection is highly dependent on the proper use of antibiotics. Additionally, various studies have demonstrated that the successful eradication of *H. pylori* is associated with a significant decrease in the incidence of duodenal ulcers<sup>1</sup>. Unfortunately, reports of antibiotic-resistant *H. pylori* isolates have been increasing, and these do not respond to currently available therapeutic regimens.

The current treatment regimen for *H. pylori* infection consists of a proton pump inhibitor (PPI) and two commonly used antibiotics, such as metronidazole and amoxicillin or clarithromycin. As well, various other antibiotics have been suggested for use in combination with PPIs, including furazolidone, erythromycin, and tetracycline<sup>2,3</sup>.

Treatment of *H. pylori* infection with commonly available antibiotics is typically recommended for several digestive conditions, including peptic ulcers<sup>4</sup>. Although various antibiotics are used to treat *H. pylori* infections globally, current data indicates an increasing resistance to most traditional drugs<sup>5</sup>.

Unfortunately, the efficacy of the recommended regimens has declined to an unacceptable level, and high antibiotic resistance rates have been reported among *H. pylori* strains isolated in northern Iran. The purpose of this report is to describe the case of a 31-year-old woman with two peptic ulcers in the duodenal antrum, who carried an *H. pylori* isolate that was resistant to seven antibiotics.

## CASE REPORT

In 2010, the presence of *H. pylori* was detected in a 31-year-old woman with gastric cancer. The *H. pylori* isolate was therefore cultured and tested for antibiotic susceptibility, using the agar dilution and disk diffusion methods<sup>6,7</sup>. Endoscopic observation indicated two 1×1cm peptic ulcers in the duodenal antrum, and there was no history of antibiotic or omeprazole use during the 5 months prior to her endoscopic surgery. Two antral biopsy specimens were obtained, and the first specimen was used for rapid urea testing (RUT) (Shim-Anzim, Iran). Within 2h of surgery, the second specimen was shipped in thioglycolate broth (Merck, Germany), within a cold-storage container, to a diagnostic laboratory.

Bacterial culture and serial plating was used to select a single, typical colony of *H. pylori*, as previously described<sup>6</sup>. Briefly, a 200µL sample of the homogenized biopsy issue was smeared on Columbia Agar plates (Merck, Germany), which were supplemented with 7% fetal calf serum and selectab tablets (MAST, UK), and incubated at 37°C under microaerophilic atmosphere for 7 days. *H. pylori* strain NCTC 11637 was used as a positive control for our susceptibility tests. Our results indicated that the patient's *H. pylori* isolate was resistant to all seven antibiotics that were tested: amoxicillin, tetracycline, clarithromycin, metronidazole, furazolidone, erythromycin, and ciprofloxacin.

**Address to:** Dr. Amin Talebi Bezmin Abadi. Heidelberglaan 100, 3584 CX, Utrecht, Netherlands.

**Phone:** 0 88 755-6507; **Fax:** 0 88 755-5426

**e-mail:** amin.talebi@gmail.com

**Received** 16 January 2014

**Accepted** 18 March 2014

## DISCUSSION

As antibiotic resistance increases, therapeutic regimens to treat *H. pylori* infections may become less effective. Given the extended use of metronidazole and clarithromycin for gastrointestinal and upper respiratory diseases, the risk of strains developing resistance may also be increasing. Thus, the emergence of the highly resistant isolate described in this case should indicate the importance of performing antibiotic susceptibility testing prior to initiating antibiotic treatment. Based on this case, clinicians should consider the possibility that all patients infected with *H. pylori* are resistant, unless data obtained from susceptibility tests indicates otherwise.

This case also highlights the need for alternative antibiotics, especially for treating patients who carry such antibiotic resistant strains. Under certain conditions, treatment regimens should be based on up-to-date, local, antibiotic resistance patterns, which can be obtained by assessing antibiotic resistance among local patients, and thus used to optimize therapeutic regimens and prevent treatment failure. Remarkably, the success of antibiotic treatments for *H. pylori* infection is affected by the possible occurrence of resistance phenomena. The distribution of resistance among *H. pylori* strains is a major outcome of overgrowth by a small population of resistant bacteria<sup>8</sup>.

Clearly, in regions with a high rate of *H. pylori* infection, it is likely that resistant strains can be isolated from the local community. Thus, public health measures play a critical role in preventing wide spread antibiotic resistance. Clinicians have expressed considerable interest regarding the ongoing use of the current formula for *H. pylori* eradication (PPI + amoxicillin and clarithromycin or metronidazole) in Iran, although it would not be surprising if this formula were to fail in the future. Development of alternative regimens for the eradication of *H. pylori* would be an invaluable advancement, although all alternative antibiotics would need to be specifically evaluated for use in various populations.

In conclusion, this report should alert the Iranian medical community that a super-resistant *H. pylori* strain exists in the region. To prevent the spread and re-emergence of these rogue isolates, adherence to infection control recommendations, antibiotic susceptibility screening, and surveillance are all necessary. The use of antibiotics as first-line treatments may be appropriate if they are selected based on local data and susceptibility test results.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## REFERENCES

1. Tomita T, Fukuda Y, Tamura K, Tanaka J, Hida N, Kosaka T, et al. Successful eradication of *Helicobacter pylori* prevents relapse of peptic ulcer disease. *Aliment Pharmacol Ther* 2002; 16 (supl II): 204-209.
2. O'Connor A, Molina-Infante J, Gisbert JP, O'Morain C. Treatment of *Helicobacter pylori* infection. *Helicobacter* 2013; 18 (supl I):58-65.
3. Georgopoulos SD, Papastergiou V, Karatapanis S. Current options for the treatment of *Helicobacter pylori*. *Expert Opin Pharmacother* 2013; 14:211-223.
4. Delahay RM, Ruge M. Pathogenesis of *Helicobacter pylori* infection. *Helicobacter* 2012; 17 (supl I):9-15.
5. Selgrad M, Malfertheiner P. Commentary: is *Helicobacter pylori* antibiotic resistance surveillance needed and how can it be delivered? *Aliment Pharmacol Ther* 2012; 36:197-199.
6. Ricci C, Holton J, Vaira D. Diagnosis of *Helicobacter pylori*: invasive and non-invasive tests. *Best Pract Res Clin Gastroenterol* 2007; 21: 299-313.
7. Talebi Bezmin Abadi A, Mobarez AM, Taghvaei T, Wolfram L. Antibiotic resistance of *Helicobacter pylori* in Mazandaran, North of Iran. *Helicobacter* 2010; 15:505-509.
8. Graham DY. Antibiotic resistance in *Helicobacter pylori*: implications for therapy. *Gastroenterol* 1998; 115:1272-1277.